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FILE 'HOME' ENTERED AT 09:24:40 ON 25 FEB 2004

=> file biosis medline caplus wpids uspatfull
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'BIOSIS' ENTERED AT 09:25:01 ON 25 FEB 2004
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FILE 'MEDLINE' ENTERED AT 09:25:01 ON 25 FEB 2004

FILE 'CAPLUS' ENTERED AT 09:25:01 ON 25 FEB 2004
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FILE 'WPIDS' ENTERED AT 09:25:01 ON 25 FEB 2004
COPYRIGHT (C) 2004 THOMSON DERWENT

FILE 'USPATFULL' ENTERED AT 09:25:01 ON 25 FEB 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

*** YOU HAVE NEW MAIL ***

=> s dye (3a) label? (4a) ribonucleotide?
L1 12 DYE (3A) LABEL? (4A) RIBONUCLEOTIDE?

=> s l1 and cleav? (5a) (primer extension? or template?)
L2 0 L1 AND CLEAV? (5A) (PRIMER EXTENSION? OR TEMPLATE?)

=> s l1 and plurality (5a) fragment?
L3 0 L1 AND PLURALITY (5A) FRAGMENT?

=> s l1 and fragment?
L4 4 L1 AND FRAGMENT?

=> d 14 bib abs 1-4

L4 ANSWER 1 OF 4 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-229331 [22] WPIDS
DNC C2003-058889
TI New **dye-labeled ribonucleotide** triphosphate
analogs useful for DNA sequencing by polymerase chain reaction.
DC B02 B03 B04 D16 E24
IN FISHER, P V; KHAN, S H; VATTA, P
PA (FISH-I) FISHER P V; (KHAN-I) KHAN S H; (VATT-I) VATTA P; (PEKE) PE CORP
NY
CYC 100
PI WO 2003000841 A2 20030103 (200322)* EN 48p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
US 2003013089 A1 20030116 (200322)
ADT WO 2003000841 A2 WO 2002-US16587 20020621; US 2003013089 A1 US 2001-886011
20010622
PRAI US 2001-886011 20010622
AN 2003-229331 [22] WPIDS

AB WO2003000841 A UPAB: 20030402

NOVELTY - Dye-labeled ribonucleotide
triphosphate analogs, are new.

DETAILED DESCRIPTION - Dye-labeled

ribonucleotide triphosphate analogs of formula (I) are new.

B' = nucleobase;

L = linker;

R3 = triphosphate, alpha -thiotriphosphate or its salt; and

T = reporter group.

INDEPENDENT CLAIMS are also included for:

(1) determining the sequence of a DNA template comprising:

(a) annealing at least one oligonucleotide primer to a template;

(b) incubating the oligonucleotide primer with a DNA polymerase that can incorporate both deoxynucleotides (dNTPs) in a reaction comprising a mixture (a1) of unlabeled dNTPs and at least one **dye-labeled ribonucleotide** to form primer extension

products;

(c) treating the primer extension products with a device (A) for hydrolyzing the extension products at each occurrence of a ribonucleotide;

(d) separating the resulting **fragments** that contain the at least one primer from other **fragments**;

(e) resolving the primer-containing extension product by size; and

(f) detecting the **fragments**;

(2) detecting mutations in DNA comprising:

(a) annealing two oligonucleotide primers to a template;

(b) incubating the two oligonucleotide primers with a DNA polymerase that can incorporate both dNTPs in a reaction comprising (a) to form primer extension products;

(c) treating the primer extension products with (A) to produce **fragments**;

(d) resolving the **fragments** by size; and

(e) detecting the **fragments**;

(3) preparation of polynucleotide **fragments** comprising:

(a) incubating the DNA template with the DNA polymerase, dATP, dGTP, dCTP, dTTP, at least two oligonucleotide primers complementary to the DNA template and (I) so that the primers are extended and the **dye-labeled ribonucleotide** is incorporated in the primer extension products and hydrolyzing 3'-5'-phosphodiester linkages between adjacent ribo- and deoxyribonucleotides;

(4) preparation of dye-labeled RNA complementary to a sequence of interest comprising preparing a mixture of a template, RNA polymerase, rATP, rGTP, rCTP, rUTP and at least one (I) oligonucleotide primers complementary to the DNA template (the sequence of interest is operable linked to a site for the initiation of RNA synthesis by the RNA polymerase), and incubating the mixture so that the RNA polymerase catalyzes the synthesis of RNA; and

(5) detection 5-methylcytosine in the DNA-template comprising:

(a) treating the template with a bisulfite salt such that 5-methylcytosine remains non-reactive;

(b) incubating the DNA template with the DNA polymerase, dATP, dGTP, dCTP, dTTP, at least two oligonucleotide primers complementary to the DNA template and a dye-labeled rCTP compound so that the primers are extended and the dye-labeled rCTP compound is incorporated in the primer extension products;

(c) hydrolyzing 3'-5'-phosphodiester linkages between adjacent ribo- and deoxyribonucleotides to produce **fragments**; resolving the **fragments** by size and detecting the **fragments**.

USE - For determining the sequence of a DNA template, for detecting mutations (e.g. single nucleotide polymorphism) in DNA (e.g. genomic DNA) and for detection of 5-methylcytosine in the DNA template, and for preparing dye-labeled RNA complementary to a sequence of interest (all claimed). As hybridization probes and in the synthesis of dye-labeled RNAs

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which are useful in quantifying the yield from an in vitro RNA synthesis and for preparing antisense and/or sense probes for in situ hybridization. Also for direct PCR sequencing.

ADVANTAGE - The compounds are efficiently incorporated into primer extension products by modified thermostable DNA polymerase.

Dwg. 0/4

L4 ANSWER 2 OF 4 USPATFULL on STN
AN 2003:17337 USPATFULL
TI **Dye-labeled ribonucleotide triphosphates**
IN Fisher, Peter Virgil, El Granada, CA, UNITED STATES
Vatta, Paolo, San Mateo, CA, UNITED STATES
Khan, Shaheer H., Foster City, CA, UNITED STATES
PI US 2003013089 A1 20030116
AI US 2001-886011 A1 20010622 (9)
DT Utility
FS APPLICATION
LREP FINNEGAN, HENDERSON, FARABOW, GARRETT &, DUNNER LLP, 1300 I STREET, NW,
WASHINGTON, DC, 20006
CLMN Number of Claims: 123
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 2302

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides novel **dye-labeled**
ribonucleotide analogs and methods for synthesizing those
analog. The compounds of the invention are especially useful for DNA
sequencing by the polymerase chain reaction.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 3 OF 4 USPATFULL on STN
AN 1999:117267 USPATFULL
TI Method of screening to find new antibiotics
IN Mankin, Alexander, Oak Park, IL, United States
PA The Board of Trustees of the University of Illinois, IL, United States
(U.S. corporation)
PI US 5958695 19990928
AI US 1998-7897 19980115 (9)
DT Utility
FS Granted
EXNAM Primary Examiner: Ketter, James
LREP Bierman, Muserlian and Lucas
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 357

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An easily automated method of screening for antibiotics active against
erythromycin resistant strains, comprising footprinting an antibiotic on
the domain II of 23S rRNA, isolating rRNA by incubating an antibiotic
with ribosomes, modifying ribosomes with a chemical modifying agent,
isolating modified rRNA and subjecting it to the reverse
transcriptase-mediated primer extension and gel electrophoresis on a DNA
sequencer to determine the extent of antibiotic-induced protection of an
rRNA nucleotide from chemical modification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 4 OF 4 USPATFULL on STN
AN 1998:27911 USPATFULL
TI Alternative **dye-labeled ribonucleotides**,

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deoxyribonucleotides, and dideoxyribonucleotides for automated DNA analysis
IN Metzker, Michael L., Houston, TX, United States
Gibbs, Richard A., Houston, TX, United States
PA Baylor College Of Medicine, Houston, TX, United States (U.S. corporation)
PI US 5728529 19980317
AI US 1995-553936 19951106 (8)
RLI Continuation-in-part of Ser. No. US 1995-494216, filed on 23 Jun 1995, now patented, Pat. No. US 5614386
DT Utility
FS Granted
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Rees, Dianne
LREP Fulbright & Jaworski L.L.P.
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 940
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the use of a class of dyes for improved DNA sequencing by the chain termination method of DNA sequencing, and internal labelling of polynucleotides by enzymatic incorporation of fluorescently-labeled ribonucleotides or deoxyribonucleotides are provided. A new class of dyes, BODIPY® fluorophores, has been described recently. The parent heterocyclic molecule of the BODIPY® fluorophores is a dipyrrometheneboron difluoride compound which is modified to create a broad class of spectrally-discriminating fluorophores. BODIPY® fluorophores have improved spectral characteristics compared to conventional fluorescein and rhodamine dyes. BODIPY® fluorophores have narrower band width, insensitivity to solvent or pH, and improved photostability, thus, BODIPY® fluorophores lead to improved DNA sequencing and/or detection in any method where electrophoresis and detection of DNA is required. Additionally, the spectral properties of the BODIPY® fluorophores are sufficiently similar in wavelength and intensity to be used with conventional equipment known in the art.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:25:01 ON
25 FEB 2004

L1 12 S DYE (3A) LABEL? (4A) RIBONUCLEOTIDE?
L2 0 S L1 AND CLEAV? (5A) (PRIMER EXTENSION? OR TEMPLATE?)
L3 0 S L1 AND PLURALITY (5A) FRAGMENT?
L4 4 S L1 AND FRAGMENT?

=> s l1 not l4

L5 8 L1 NOT L4

=> dup rem l5

PROCESSING COMPLETED FOR L5

L6 7 DUP REM L5 (1 DUPLICATE REMOVED)

=> d 16 bib abs 1-7

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1007111 CAPLUS

DN 140:54444

TI Methods and kit for labeling dsRNA and siRNA molecules that reduce gene
expression through RNA interference

IN Ford, Lance P.; Byrom, Mike; Pasloske, Brittan L.

PA Ambion, Inc., USA

SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003106631	A2	20031224	WO 2003-US18627	20030612
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004029275	A1	20040212	US 2002-298480	20021115
	US 2004033602	A1	20040219	US 2003-460775	20030612
PRAI	US 2002-360772	A1	20020612		
	US 2002-402347P	P	20020810		
AB	The present invention concerns methods and compns. involving labeled, doublestranded RNA (dsRNA), including siRNA, capable of triggering RNA-mediated interference (RNAi) in a cell. Compns. of the invention include labeled dsRNA for RNAi, which may be a single strand of RNA that basepairs with itself or two sep. RNA strands. In some embodiments, the label is fluorescent. The present invention further concerns methods for preparing such composition and kits for implementing such methods. Other methods of the invention include ways of using labeled dsRNA for RNAi. In particular embodiments, dsRNA or siRNA fluorescently labeled internally, at 5'-end, or in its minor groove specific to c-myc, GAPDH, and Drosophila				

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Hrp48 or U2Af50, are shown to reduce their corresponding gene expression in Hela cells or Drosophila L2 cells as effectively as unlabeled siRNA. The attachment of fluorescent label to RNA mols. are useful to analyze the cellular distribution of siRNA and elucidate the mechanism of RNAi. Also discussed are attachment of other bulky groups to siRNA and the tests for their effects on siRNA activity.

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:6086 CAPLUS
DN 138:67806
TI **Dye-labeled ribonucleotide triphosphates for use in DNA sequencing and detection of mutations or 5-methylcytosine in DNA**
IN Fisher, Peter Virgil; Vatta, Paolo; Khan, Shaheer H.
PA PE Corporation (NY), USA; Applera Corp.
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000841	A2	20030103	WO 2002-US16587	20020621
	WO 2003000841	A3	20031106		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003013089	A1	20030116	US 2001-886011	20010622
PRAI	US 2001-886011	A	20010622		
OS	MARPAT	138:67806			
AB	The invention provides novel dye-labeled ribonucleotide analogs and methods for synthesizing those analogs. The compds. of the invention are especially useful for DNA sequencing by the polymerase chain reaction. Thus, ribonucleoside triphosphate labeled with ROX, R6G, TAMRA, and R110 were prepared and used in PCR sequencing of DNA, PCR detection of SNPs, and in determination of the methylation state of DNA.				
The	fluorophores were attached to the 7 position of 7-deazapurines and to the 5 position of pyrimidines via propargylamine or propargyloxyethylamine linkers.				

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ECL -- Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 1991

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods of screening for compounds that bind RNA molecules. In particular, the methods of the invention comprise screening a library of test compounds, each of which is attached to a solid support, with a dye-labeled RNA molecule to form a dye-labeled target RNA: support-attached test compound complex. By virtue of the dye label on the target RNA, the support becomes labeled and can be separated from unlabeled solid supports. The present invention further relates to methods of inhibiting an RNA-protein interaction, to methods of screening for compounds that increase or decrease the production of a protein, and to methods of screening for a compound that is capable of treating or preventing a disease whose progression is associated with an in vivo binding of a test compound to a target RNA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 7 USPATFULL on STN
AN 2003:6797 USPATFULL
TI Methods for identifying RNA binding compounds
IN Rana, Tariq M, Piscataway, NJ, United States
PA University of Medicine and Dentistry of New Jersey, New Brunswick, NJ, United States (U.S. corporation)
PI US 6503713 B1 20030107
AI US 2000-679451 20001004 (9)
PRAI US 1999-157646P 19991004 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Riley, Jezia
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 50
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 2033

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods of screening for compounds that bind RNA molecules. In particular, the methods of the invention comprise screening a library of test compounds, each of which is attached to a solid support, with a dye-labeled RNA molecule to form a dye-labeled target RNA: support-attached test compound complex. By virtue of the dye label on the target RNA, the support becomes labeled and can be separated from unlabeled solid supports. The present invention further relates to methods of inhibiting an RNA-protein interaction, to methods of screening for compounds that increase or decrease the production of a protein, and to methods of screening for a compound that is capable of treating or preventing a disease whose progression is associated with an in vivo binding of a test compound to a target RNA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 5 OF 7 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-169204 [15] WPIDS
DNC C1999-049644
TI New recombinant thermostable DNA polymerase - able to incorporate nucleotides labelled with fluorescin family dyes.
DC B04 D16
IN GELFAND, D H; KALMAN, L V; MYERS, T W; REICHERT, F L; SIGUA, C L; RELCHERT, F L
PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (GELF-I) GELFAND D H; (KALM-I) KALMAN L V; (MYER-I) MYERS T W; (REIC-I) REICHERT F L; (SIGU-I) SIGUA C L

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CYC 37
PI EP 902035 A2 19990317 (199915)* EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
CZ 9802874 A3 19990317 (199917)
NO 9804157 A 19990312 (199920)
AU 9884161 A 19990325 (199924)
HU 9802024 A2 19990528 (199930)
JP 11137284 A 19990525 (199931) 28p
CA 2243985 A1 19990311 (199934) EN
CN 1218832 A 19990609 (199941)
BR 9803419 A 20000208 (200023)
KR 99029676 A 19990426 (200028)
MX 9807358 A1 19991101 (200106)
AU 741366 B 20011129 (200206)
US 6346379 B1 20020212 (200219)
US 2002142333 A1 20021003 (200267)
TW 513439 A 20021211 (200353)
US 2003152988 A1 20030814 (200355)
ADT EP 902035 A2 EP 1998-116786 19980905; CZ 9802874 A3 CZ 1998-2874 19980909;
NO 9804157 A NO 1998-4157 19980910; AU 9884161 A AU 1998-84161 19980910;
HU 9802024 A2 HU 1998-2024 19980907; JP 11137284 A JP 1998-258414
19980911; CA 2243985 A1 CA 1998-2243985 19980903; CN 1218832 A CN
1998-124526 19980911; BR 9803419 A BR 1998-3419 19980910; KR 99029676 A KR
1998-37299 19980910; MX 9807358 A1 MX 1998-7358 19980910; AU 741366 B AU
1998-84161 19980910; US 6346379 B1 Provisional US 1997-58525P 19970911, US
1998-146631 19980903; US 2002142333 A1 Provisional US 1997-58525P
19970911, Cont of US 1998-146631 19980903, US 2002-52417 20020117; TW
513439 A TW 1998-114826 19980907; US 2003152988 A1 Provisional US
1997-58525P 19970911, Cont of US 1998-146631 19980903, Cont of US
2002-52417 20020117, US 2003-355532 20030130
FDT AU 741366 B Previous Publ. AU 9884161; US 2003152988 A1 Cont of US 6346379
PRAI US 1997-58525P 19970911; US 1998-146631 19980903; US 2002-52417
20020117; US 2003-355532 20030130
AN 1999-169204 [15] WPIDS
AB EP 902035 A UPAB: 19990416
NOVELTY - A recombinant thermostable DNA polymerase (pol) mutated at
position 4 (not to Glu) has a reduced level of discrimination against
incorporation of nucleotides labelled with fluorescin family dyes in
comparison to the native.
DETAILED DESCRIPTION - The native polymerase has sequence (I), (II)
or (III):
Leu Ser Xaa3 Xaa4 Leu Xaa6 Xaa7 Pro Xaa9 Xaa10 Glu (I)
where: Xaa = any amino amino acid residue, except Xaa7 = Val or
Ile;
Leu Ser Xaa3 Xaa4 Leu Xaa6 Lle Pro Tyr Glu Glu (II)
where: Xaa3 = Gln or Gly; Xaa4 = any amino acid; and Xaa6 = Ser or
Ala; and
Leu Ser Val Xaa4 Leu Gly Xaa7 Pro Val Lys Glu (III)
where: Xaa4 = any amino acid, preferably Arg; and Xaa7 = Val or Ile.
INDEPENDENT CLAIMS are included for the following: (1) a nucleic acid
encoding the pol; (2) a vector comprising the nucleic acid; (3) a host
cell comprising the nucleic acid; (4) preparation of pol; and (5) kits
for: (i) DNA sequencing; (ii) producing labelled DNA; and (iii) producing
labelled primer extension products; comprising pol and a terminator,
nucleotide and ribonucleotide respectively, labelled with a
negatively-charged fluorescent dye.
USE - Pol is useful in in vitro DNA synthesis applications, including
DNA sequencing, synthesis of labelled DNA and production of labelled
primer products (claimed). Pol (III) also comprising (IV): SQIXLR(V/I)
(IV) where X - any amino acid except E; and a **ribonucleotide**
labelled with a fluorescin **dye**; is preferred for

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production of labelled primer extension products (claimed). Pol was used in automated sequencing with fluorescin dye labelled dideoxynucleotides, resulting in accuracy of greater than 98.5%.

ADVANTAGE - The new pol efficiently incorporates conventional and fluorescin-labelled nucleotides, has an increased rate of primer extension, and has increased uniformity of incorporation of the various terminator nucleotides, compared to prior art DNA polymerases. The new pol uses lower concentrations of fluorescin dye family-labelled dideoxynucleotides (ddNTPs) (lower cost), and lower ratios of labelled ddNTPs to dNTPs (more efficient polymerization, lower concentrations of template needed, decreased likelihood of introducing inhibitors). Long templates are more easily sequenced, and sequencing products can be loaded directly onto sequencing gels without prior purification.

Dwg.0/1

L6 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
AN 2002:104663 BIOSIS
DN PREV200200104663
TI Alternative **dye-labeled ribonucleotides**,
deoxyribonucleotides, and dideoxyribonucleotides for automated DNA
analysis.
AU Metzker, M. L. [Inventor]; Gibbs, R. A. [Inventor]
CS Houston, Tex., USA
ASSIGNEE: BAYLOR COLLEGE OF MEDICINE
PI US 5728529 March 17, 1998
SO Official Gazette of the United States Patent and Trademark Office Patents,
(March 17, 1998) Vol. 1208, No. 3, pp. 2315-2316. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DT Patent
LA English
ED Entered STN: 24 Jan 2002
Last Updated on STN: 25 Feb 2002

L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:172504 CAPLUS
DN 126:167460
TI Alternative **dye-labeled primers**,
ribonucleotides, deoxyribonucleotides, and dideoxyribonucleotides
for automated DNA analysis and homogeneous amplification/detection assays.
IN Metzker, Michael L.; Gibbs, Richard A.
PA Baylor College of Medicine, USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9700967	A1	19970109	WO 1996-US10729	19960621
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5614386	A	19970325	US 1995-494216	19950623
	US 5861287	A	19990119	US 1995-540228	19951006
	US 5728529	A	19980317	US 1995-553936	19951106
	US 5994063	A	19991130	US 1996-612036	19960307
	AU 9662886	A1	19970122	AU 1996-62886	19960621
	AU 699939	B2	19981217		
	EP 833936	A1	19980408	EP 1996-921749	19960621
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1995-494216		19950623		

09567863

US 1995-540228	19951006
US 1995-553936	19951106
US 1996-612036	19960307
WO 1996-US10729	19960621

AB Methods for the use of a class dyes for improved DNA sequencing are provided. A new class of dyes, BODIPY® fluorophores, has been described recently. The parent heterocyclic mol. of the BODIPY® fluorophores is a dipyrrometheneboron difluoride compound which is modified to create a broad class of spectrally-discriminating fluorophores. The present invention provides methods for the use of BODIPY® fluorophore-labeled DNA for dye-primer sequencing in which the BODIPY®'s are attached to the 5' end of sequencing by enzymic incorporation of fluorescently-labeled ribonucleotides or deoxyribonucleotides, and provides oligonucleotides labeled with substituted 4,4-difluoro-4-bora-3A,4A-diaza-s-indacene (BODIPY® fluorophore) compds. for performing the Taqman assay. BODIPY® fluorophores have improved spectral characteristics compared to conventional fluorescein and rhodamine dyes. BODIPY® fluorophores have narrower band width, insensitivity to solvent or pH, and improved photostability; thus, BODIPY® fluorophores lead to improved DNA sequencing and/or detection in any method where electrophoresis and detection of DNA is required. Addnl., the spectral properties of the BODIPY® fluorophores are sufficiently similar in wavelength and intensity to be used with conventional equipment known in the art.

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FILE 'HOME' ENTERED AT 10:12:49 ON 25 FEB 2004

=> file biosis medline caplus wpids uspatfull
COST IN U.S. DOLLARS

SINCE FILE ENTRY	2.52	TOTAL SESSION	2.52
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FILE 'WPIDS' ENTERED AT 10:19:47 ON 25 FEB 2004
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FILE 'USPATFULL' ENTERED AT 10:19:47 ON 25 FEB 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

*** YOU HAVE NEW MAIL ***

=> s dye (3a) label? (4a) ribonucleotide?
L1 12 DYE (3A) LABEL? (4A) RIBONUCLEOTIDE?

=> S 11 and cleav?
L2 3 L1 AND CLEAV?

=> d 12 bib abs 1-3

L2 ANSWER 1 OF 3 USPATFULL on STN
AN 2003:220232 USPATFULL
TI Methods for identifying RNA binding compounds
IN Rana, Tariq M., Piscataway, NJ, UNITED STATES
PA University of Medicine and Dentistry of New Jersey, New Brunswick, NJ
(U.S. corporation)
PI US 2003153523 A1 20030814
AI US 2002-295761 A1 20021115 (10)
RLI Continuation of Ser. No. US 2000-679451, filed on 4 Oct 2000, GRANTED,
Pat. No. US 6503713
PRAI US 1999-157646P 19991004 (60)
DT Utility
FS APPLICATION
LREP PENNIE AND EDMONDS, 1155 AVENUE OF THE AMERICAS, NEW YORK, NY, 100362711
CLMN Number of Claims: 62
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 1991
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods of screening for compounds that bind RNA molecules. In particular, the methods of the invention comprise screening a library of test compounds, each of which is attached to a solid support, with a dye-labeled RNA molecule to form a dye-labeled target RNA:support-attached test compound complex. By virtue of the dye label on the target RNA, the support becomes labeled and can be separated from unlabeled solid supports. The present invention further relates to methods of inhibiting an RNA-protein interaction, to methods of screening for compounds that increase or decrease the production of a

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protein, and to methods of screening for a compound that is capable of treating or preventing a disease whose progression is associated with an in vivo binding of a test compound to a target RNA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 2 OF 3 USPATFULL on STN
AN 2003:17337 USPATFULL
TI **Dye-labeled ribonucleotide triphosphates**
IN Fisher, Peter Virgil, El Granada, CA, UNITED STATES
Vatta, Paolo, San Mateo, CA, UNITED STATES
Khan, Shaheer H., Foster City, CA, UNITED STATES
PI US 2003013089 A1 20030116
AI US 2001-886011 A1 20010622 (9)
DT Utility
FS APPLICATION
LREP FINNEGAN, HENDERSON, FARABOW, GARRETT &, DUNNER LLP, 1300 I STREET, NW,
WASHINGTON, DC, 20006
CLMN Number of Claims: 123
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 2302
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides novel **dye-labeled**
ribonucleotide analogs and methods for synthesizing those
analog. The compounds of the invention are especially useful for DNA
sequencing by the polymerase chain reaction.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 3 OF 3 USPATFULL on STN
AN 2003:6797 USPATFULL
TI Methods for identifying RNA binding compounds
IN Rana, Tariq M, Piscataway, NJ, United States
PA University of Medicine and Dentistry of New Jersey, New Brunswick, NJ,
United States (U.S. corporation)
PI US 6503713 B1 20030107
AI US 2000-679451 20001004 (9)
PRAI US 1999-157646P 19991004 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Riley, Jezia
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 50
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 2033
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods of screening for compounds that bind RNA molecules. In particular, the methods of the invention comprise screening a library of test compounds, each of which is attached to a solid support, with a dye-labeled RNA molecule to form a dye-labeled target RNA:support-attached test compound complex. By virtue of the dye label on the target RNA, the support becomes labeled and can be separated from unlabeled solid supports. The present invention further relates to methods of inhibiting an RNA-protein interaction, to methods of screening for compounds that increase or decrease the production of a protein, and to methods of screening for a compound that is capable of treating or preventing a disease whose progression is associated with an in vivo binding of a test compound to a target RNA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 12 3 kwic

L2 ANSWER 3 OF 3 USPATFULL on STN

DETD . . . and the cycle is repeated one or more times until chain elongation is complete. After synthesis, the polynucleotide chain is **cleaved** from the support using a base, e.g., ammonium hydroxide or t-butyl amine. The **cleavage** reaction also removes any phosphate protecting groups, e.g., cyanoethyl. Finally, the protecting groups on the exocyclic amines of the bases. . . .

DETD . . . template-directed enzymatic extension of the primed template (e.g., a mixture including GTP, ATP, CTP, and UTP), including one or more **dye-labeled ribonucleotides** (Sigma-Aldrich, St. Louis, Mo.), is added to the primed template. Next, a polymerase enzyme is added to the mixture under. . . .

DETD . . . providing points of test compound attachment to the solid support, but also for allowing different groups of molecules to be **cleaved** from the solid support under different conditions, depending on the nature of the linker. For example, linkers can be, *inter alia*, electrophilically **cleaved**, nucleophilically **cleaved**, photocleavable, enzymatically **cleaved**, **cleaved** by metals, **cleaved** under reductive conditions or **cleaved** under oxidative conditions. In embodiments where readable molecular tags are **cleaved** from the solid support and analyzed to determine the structure of the library compound on the support (see below), the. . . be attached to the solid support via one or more different types of linkers, such that the tags can be **cleaved** without removing the test compound from the support, and vice versa. Appropriate types of linkers useful in embodiments of the. . . .

DETD . . . itself is determined using, e.g., nuclear magnetic resonance ("NMR") spectroscopy of the test compound either on the support or after **cleavage**, then, as used herein, the test compound is the readable tag. These embodiments of the invention use direct techniques for. . . .

DETD . . . spinning NMR spectroscopy (Warrass et al. (1999) J. Am. Chem. Soc. 121:3787-3788). In these embodiments, the test compounds are not **cleaved** from the solid support, thus eliminating an extra chemistry step that may destroy them. Instead, NMR spectra of support-bound test. . . .

DETD . . . mass spectrometry methods are sensitive methods requiring only small amounts of sample that can be the test compounds either after **cleavage** or while on the solid support. In yet other embodiments, X-ray photoelectron spectroscopy is used to identify the structure of. . . .

DETD . . . tags provide a history of the synthesis as well as identify the test compound on the support. The tags are **cleaved** from the solid support and read by, e.g., electron capture gas chromatography, in order to decode the support. Different types. . . .

DETD . . . 16 mM sodium citrate, pH 5.0, 0.8 mM EDTA, 0.5 mg/ml yeast tRNA (Gibco-BRL). This enzyme yields U- and C-specific **cleavage** of RNA. Sequencing products were resolved on 20% denaturing gels and visualized by phosphor image analysis.

DETD . . . 350 nm for 4 hours and spun for 5 minutes in a centrifuge. The capillary tube was opened and the **cleaved** tag alcohols were silylated with N, O-bis(trimethylsilyl)acetamide in a micro syringe. The N, O-bis(trimethylsilyl)acetamide derivatives (1 μ L) were analyzed using. . . .

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UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003013089 A1 20030116 US 2001-886011 20010622

PRAI US 2001-886011 A 20010622

OS MARPAT 138:67806

AB The invention provides novel **dye-labeled ribonucleotide** analogs and methods for synthesizing those analogs. The compds. of the invention are especially useful for DNA sequencing by the polymerase chain reaction. Thus, ribonucleoside triphosphate labeled with ROX, R6G, TAMRA, and R110 were prepared and used in PCR sequencing of DNA, PCR detection of SNPs, and in determination of the methylation state of DNA.

The fluorophores were attached to the 7 position of 7-deazapurines and to the 5 position of pyrimidines via propargylamine or propargyloxyethylamine linkers.

L2 ANSWER 2 OF 2 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-229331 [22] WPIDS

DNC C2003-058889

TI New **dye-labeled ribonucleotide** triphosphate analogs useful for **DNA sequencing** by polymerase chain reaction.

DC B02 B03 B04 D16 E24

IN FISHER, P V; KHAN, S H; VATTA, P

PA (FISH-I) FISHER P V; (KHAN-I) KHAN S H; (VATT-I) VATTA P; (PEKE) PE CORP
NY

CYC 100

PI WO 2003000841 A2 20030103 (200322)* EN 48p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

US 2003013089 A1 20030116 (200322)

ADT WO 2003000841 A2 WO 2002-US16587 20020621; US 2003013089 A1 US 2001-886011
20010622

PRAI US 2001-886011 20010622

AN 2003-229331 [22] WPIDS

AB WO2003000841 A UPAB: 20030402

NOVELTY - **Dye-labeled ribonucleotide** triphosphate analogs, are new.

DETAILED DESCRIPTION - **Dye-labeled**

ribonucleotide triphosphate analogs of formula (I) are new.

B' = nucleobase;

L = linker;

R3 = triphosphate, alpha -thiotriphosphate or its salt; and

T = reporter group.

INDEPENDENT CLAIMS are also included for:

(1) determining the sequence of a DNA template comprising:
(a) annealing at least one oligonucleotide primer to a template;
(b) incubating the oligonucleotide primer with a DNA polymerase that can incorporate both deoxynucleotides (dNTPs) in a reaction comprising a mixture (a1) of unlabeled dNTPs and at least one **dye-labeled ribonucleotide** to form primer extension products;

(c) treating the primer extension products with a device (A) for hydrolyzing the extension products at each occurrence of a ribonucleotide;
(d) separating the resulting fragments that contain the at least one primer from other fragments;

- (e) resolving the primer-containing extension product by size; and
- (f) detecting the fragments;

(2) detecting mutations in DNA comprising:

- (a) annealing two oligonucleotide primers to a template;
- (b) incubating the two oligonucleotide primers with a DNA polymerase that can incorporate both dNTPs in a reaction comprising (a) to form primer extension products;
- (c) treating the primer extension products with (A) to produce fragments;
- (d) resolving the fragments by size; and
- (e) detecting the fragments;

(3) preparation of polynucleotide fragments comprising:

- (a) incubating the DNA template with the DNA polymerase, dATP, dGTP, dCTP, dTTP, at least two oligonucleotide primers complementary to the DNA template and (I) so that the primers are extended and the **dye-labeled ribonucleotide** is incorporated in the primer extension products and hydrolyzing 3'-5'-phosphodiester linkages between adjacent ribo- and deoxyribonucleotides;
- (4) preparation of dye-labeled RNA complementary to a sequence of interest comprising preparing a mixture of a template, RNA polymerase, rATP, rGTP, rCTP, rUTP and at least one (I) oligonucleotide primers complementary to the DNA template (the sequence of interest is operable linked to a site for the initiation of RNA synthesis by the RNA polymerase), and incubating the mixture so that the RNA polymerase catalyzes the synthesis of RNA; and
- (5) detection 5-methylcytosine in the DNA-template comprising:
 - (a) treating the template with a bisulfite salt such that 5-methylcytosine remains non-reactive;
 - (b) incubating the DNA template with the DNA polymerase, dATP, dGTP, dCTP, dTTP, at least two oligonucleotide primers complementary to the DNA template and a dye-labeled rCTP compound so that the primers are extended and the dye-labeled rCTP compound is incorporated in the primer extension products;
 - (c) hydrolyzing 3'-5'-phosphodiester linkages between adjacent ribo- and deoxyribonucleotides to produce fragments; resolving the fragments by size and detecting the fragments.

USE - For determining the sequence of a DNA template, for detecting mutations (e.g. single nucleotide polymorphism) in DNA (e.g. genomic DNA) and for detection of 5-methylcytosine in the DNA template, and for preparing dye-labeled RNA complementary to a sequence of interest (all claimed). As hybridization probes and in the synthesis of dye-labeled RNAs which are useful in quantifying the yield from an in vitro RNA synthesis and for preparing antisense and/or sense probes for in situ hybridization. Also for direct PCR sequencing.

ADVANTAGE - The compounds are efficiently incorporated into primer extension products by modified thermostable DNA polymerase.

Dwg.0/4

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=> s label? (2a) ribonucleotide?
L1 403 LABEL? (2A) RIBONUCLEOTIDE?

=> s l1 and cleav? (4a) extension (4a) product?
L2 4 L1 AND CLEAV? (4A) EXTENSION (4A) PRODUCT?

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 4 DUP REM L2 (0 DUPLICATES REMOVED)

=> d l3 bib abs 1-4

L3 ANSWER 1 OF 4 USPATFULL on STN
AN 2003:194479 USPATFULL
TI Method for identifying polymorphisms
IN Stanton, Vince P., JR., Belmont, MA, UNITED STATES
Wolfe, Jia Liu, Winchester, MA, UNITED STATES
Kawate, Tomohiko, Cambridge, MA, UNITED STATES
Verdine, Gregory L., Cambridge, MA, UNITED STATES
Olson, Jeffrey, Chelmsford, MA, UNITED STATES
PI US 2003134290 A1 20030717
AI US 2002-105101 A1 20020322 (10)
RLI Division of Ser. No. US 2000-655104, filed on 5 Sep 2000, PENDING
Continuation-in-part of Ser. No. US 1999-394467, filed on 10 Sep 1999,
PENDING Continuation-in-part of Ser. No. US 1999-394457, filed on 10 Sep
1999, GRANTED, Pat. No. US 6440705 Continuation-in-part of Ser. No. US
1999-394774, filed on 10 Sep 1999, ABANDONED Continuation-in-part of
Ser. No. US 1999-394387, filed on 10 Sep 1999, ABANDONED

PRAI US 1998-102724P 19981001 (60)

DT Utility

FS APPLICATION

LREP LYON & LYON LLP, 633 WEST FIFTH STREET, SUITE 4700, LOS ANGELES, CA,
90071

CLMN Number of Claims: 31

ECL Exemplary Claim: 1

DRWN 60 Drawing Page(s)

LN.CNT 6220

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for the detection of
polymorphism in polynucleotides by using hybridization of fragments of
segments of a polynucleotide suspected of containing a polymorphism with
an oligonucleotide having a sequence complementary to a fragment
identifying the polymorphism and subsequent detection of incorporated
labels in the oligonucleotide-fragment duplex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 2 OF 4 USPATFULL on STN
AN 2003:17337 USPATFULL
TI Dye-labeled ribonucleotide triphosphates
IN Fisher, Peter Virgil, El Granada, CA, UNITED STATES
Vatta, Paolo, San Mateo, CA, UNITED STATES
Khan, Shaheer H., Foster City, CA, UNITED STATES
PI US 2003013089 A1 20030116
AI US 2001-886011 A1 20010622 (9)
DT Utility
FS APPLICATION
LREP FINNEGAN, HENDERSON, FARABOW, GARRETT &, DUNNER LLP, 1300 I STREET, NW,
WASHINGTON, DC, 20006
CLMN Number of Claims: 123
ECL Exemplary Claim: 1

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DRWN 4 Drawing Page(s).

LN.CNT 2302

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides novel dye-labeled
ribonucleotide analogs and methods for synthesizing those
analog. The compounds of the invention are especially useful for DNA
sequencing by the polymerase chain reaction.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 3 OF 4 USPATFULL on STN

AN 2002:346801 USPATFULL

TI Method for identifying polymorphisms

IN Stanton, Jr., Vince P., Belmont, MA, United States
Wolfe, Jia Liu, Winchester, MA, United States
Kawate, Tomohiko, Cambridge, MA, United States
Verdine, Gregory L., Cambridge, MA, United States
Olson, Jeffrey, Chelmsford, MA, United States

PA Variagenics, Inc., Cambridge, MA, United States (U.S. corporation)

PI US 6500650 B1 20021231

AI US 2000-655104 20000905 (9)

RLI Continuation-in-part of Ser. No. US 1999-394467, filed on 10 Sep 1999
Continuation-in-part of Ser. No. US 1999-394457, filed on 10 Sep 1999
Continuation-in-part of Ser. No. US 1999-394774, filed on 10 Sep 1999
Continuation-in-part of Ser. No. US 1999-394387, filed on 10 Sep 1999

PRAI US 1998-102724P 19981001 (60)

US 1999-149533P 19990817 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Riley, Jezia

LREP Lyon & Lyon LLP

CLMN Number of Claims: 31

ECL Exemplary Claim: 1

DRWN 72 Drawing Figure(s); 59 Drawing Page(s)

LN.CNT 6037

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for the detection of
polymorphism in polynucleotides by using hybridization of fragments of
segments of a polynucleotide suspected of containing a polymorphism with
an oligonucleotide having a sequence complementary to a fragment
identifying the polymorphism and subsequent detection of incorporated
labels in the oligonucleotide-fragment duplex.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 4 USPATFULL on STN

AN 1999:96243 USPATFULL

TI Thermostable DNA polymerases having reduced discrimination against
ribo-NTPs

IN Gelfand, David Harrow, Oakland, CA, United States
Kalman, Lisa Vivian, San Francisco, CA, United States
Reichert, Fred Lawrence, Oakland, CA, United States

PA Roche Molecular Systems, Inc., Pleasanton, CA, United States (U.S.
corporation)

PI US 5939292 19990817

AI US 1997-906484 19970805 (8)

PRAI US 1996-23376P 19960806 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Stole, Einar

LREP Petry, Douglas A.

CLMN Number of Claims: 25

09567863

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1858

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Modified thermostable DNA polymerases having enhanced efficiency for incorporating unconventional nucleotides, such as ribonucleotides, into DNA products, are advantageous in many in vitro synthesis applications. Such enzymes are particularly useful for use in nucleic acid sequencing protocols and provide novel means for DNA sequence analysis. Genes encoding the modified enzymes and methods for their production and use offer cost and efficiency advantages for DNA sequencing.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.